Remarks

Claims 1-11, 16 and 22-26 are pending in the instant application. Applicants have hereinabove cancelled claim 3 without disclaimer or prejudice to applicants' right to pursue the subject matter of this claim in a future application. In addition, applicants have hereinabove amended claim 1. Support for these amendments may be found in the subject specification. This Amendment does not involve any issue of new matter. Therefore, entry of this Amendment is respectfully requested such that claims 1, 2, 4-11, 16 and 22-26 will be pending and under examination.

Claim Rejection Under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1-11, 16 and 22-26 under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for methods of treating certain conditions, allegedly does not reasonably provide enablement for preventing the claimed conditions.

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants point out that claim 3 has been cancelled. Thus, the rejection thereof is now moot.

In response to the Examiner's rejection of the remaining claims, applicants respectfully traverse. Nevertheless, without conceding the correctness of the Examiner's rejection and to expedite prosecution of the subject application, applicants have hereinabove amended claim 1 such that it no longer recites the term "preventing".

In light of the above amendment, applicants contend that claim 1, and claims 2, 4-11, 16 and 22-26 which depend therefrom, satisfy the enablement requirement of 35 U.S.C. §112, first paragraph. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claim Rejections Under 35 U.S.C. §102(e)

The Examiner rejected claims 1-11, 16 and 24-26 under 35 U.S.C. §102(e) as allegedly being anticipated by DiSalle et al. (WO02/72106).

In response, applicants respectfully traverse. Claim 1, as amended, provides a method for treating endometriosis in a patient in need of such treatment, *consisting of* the administration of an effective amount of a cyclooxygenase-2 selective inhibitor to said patient, wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of: rofecoxib, etoricoxib, celecoxib, valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502 and GW406381 (emphasis added).

DiSalle et al. does not teach the method of applicants' claimed invention. Specifically, DiSalle et al. teaches the treatment of endometriosis with a combination of two compounds, namely an aromatase inactivator and an additional therapeutic agent such as a COX-2 inhibitor or a GnRH agonist. Applicants' claims do not recite the combination taught in DiSalle et al. Therefore, DiSalle et al. fails to teach each and every element of amended claim 1.

In view of the above remarks, applicants maintain that claim 1, and claims 2, 4-11, 16 and 24-26 which depend therefrom, satisfy the requirements of 35 U.S.C. §102(e) and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claim Rejections Under 35 U.S.C. §103(a)

Masferrer et al. in view of Riendeau et al.

The Examiner rejected claim 16, and claims 1-11, under 35 U.S.C. §103(a) as allegedly unpatentable over Masferrer et al. (WO98/22101) in view of Riendeau et al. (*J. Pharm. Exp. Ther.* 296(2): 558-566 (2001)).

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants point out that claim 3 has been cancelled. Thus, the rejection thereof is now moot.

In response to the rejection of claim 16, and as it may apply to amended claim 1, applicants respectfully traverse and maintain that a *prima facie* case of obviousness does not exist with respect to any of the pending claims.

Claim 1 provides a method for treating endometriosis in a patient in need of such treatment, consisting of the administration of an effective amount of a cyclooxygenase-2 selective inhibitor to said patient, wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of: rofecoxib, etoricoxib, celecoxib, valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502 and GW406381. The COX-2 inhibitor under examination is etoricoxib as recited in claim 16, and the following remarks will be directed to this compound.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to the claim. First, the cited references, when combined, must teach or suggest every limitation of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

Here, the cited references fail to support a *prima facie* case of obviousness. Specifically, Masferrer et al. when combined with Riendeau et al., fail to provide a motive to combine and a reasonable expectation of success.

Masferrer et al. does not teach or suggest the specific COX-2 inhibitor under examination, namely etoricoxib or any compound having a similar structure. Instead, Masferrer et al. suggest compounds having a particular structure as set forth in formulas I and II, recited on pages 6-26 therein, for use in treating endometrisosis. The Examiner has conceded that the compounds encompassed by formulas I and II of Masferrer et al. do not include etoricoxib.

Riendeau et al. does not teach or suggest the use of etoricoxib to treat endometriosis. Riendeau et al. teach the use of etoricoxib to treat arthritis, hyperalgesia and pyresis. The use of etoricoxib to treat or prevent other diseases is unclear as evidenced on page 565, last paragraph of Riendeau et al., wherein the authors admit that further clinical studies with etoricoxib would be needed in order to explore the therapeutic potential of selective COX-2 inhibitors in inflammatory conditions, cancer and neurological disorders. Not only is the usefulness of selective COX-2 inhibitors to treat additional diseases/disorders unclear, nowhere do the authors mention the use of such inhibitors to treat endometriosis.

In addition, Masferrer et al. define a "cyclooxygenase-2 inhibitor" as "compounds which have a cyclooxygenase-2 IC_{50} of less than about 0.2 μM" (see page 5, last para). According to Riendeau, etoricoxib has an IC_{50} value of 1.1 ± 0.1 μM" (see abstract), i.e. an IC_{50} that is greater than the value taught in Masferrer et al.

As demonstrated above, there is simply no motivation to combine the cited references to create applicants' claimed invention since etoricoxib does not fall within the class of COX-2 inhibitors defined in Masferrer et al. to treat endometriosis. Riendeau does not cure the defects of Masferrer since the COX-2 inhibitor taught in Riendeau does not fall within the definition of a COX-2 inhibitor as taught by Masferrer. None of the references cited by the Examiner give any motivation to one skilled in the art with respect to the use of etoricoxib to treat endometriosis.

In view of the above remarks, applicants maintain that claims 1-11 and 16 satisfy the requirements of 35 U.S.C. §103(a). Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

DiSalle et al. in view of Heinrichs

The Examiner rejected claims 1 and 22, 23, 25 and 26 under 35 U.S.C. §103(a) as allegedly unpatentable over DiSalle et al. (WO02/72106) in view of Heinrichs (US 6,265,393, issued July 24, 2001).

In response to the rejection, applicants respectfully traverse and maintain that a *prima facie* case of obviousness does not exist with respect to any of the rejected claims.

Claim 1, as amended, provides a method for treating endometriosis in a patient in need of such treatment, *consisting of* the administration of an effective amount of a cyclooxygenase-2 selective inhibitor to said patient, wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of: rofecoxib, etoricoxib, celecoxib, valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502 and GW406381 (emphasis added).

Claim 22 provides a method for treating or preventing endometriosis in a patient in need of such treatment, consisting of the administration of an effective amount of a cyclooxygenase-2

selective inhibitor to said patient, wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of: rofecoxib, etoricoxib, celecoxib, valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502 and GW406381, and wherein the cyclooxygenase-2 selective inhibitor is concomitantly or sequentially co-administered with an oral contraceptive. The COX-2 inhibitor elected for examination is etoricoxib, and the oral contraceptive elected for examination is norethindrone as recited in claim 23.

Claim 25 provides a method for treating endometriosis in a patient in need of such treatment, consisting of the administration of an effective amount of a cyclooxygenase-2 selective inhibitor to said patient, wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of: rofecoxib, etoricoxib, celecoxib, valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502 and GW406381, and wherein the cyclooxygenase-2 selective inhibitor is concomitantly or sequentially co-administered with a GnRH-agonist. The COX-2 inhibitor elected for examination is etoricoxib, and the GnRH-agonist elected for examination is leuprolide acetate as recited in claim 26.

The following remarks will be directed to these compounds.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to the claim. First, the cited references, when combined, must teach or suggest every limitation of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

Here, the cited references fail to support a *prima facie* case of obviousness. Specifically, DiSalle et al. when combined with Heinrichs, fail to provide a motive to combine and a reasonable expectation of success.

As previously discussed *supra*, DiSalle et al. does not teach the method of applicants' claimed invention. Specifically, DiSalle et al. teaches the treatment of endometriosis with a combination of two compounds, namely an aromatase inactivator and an additional therapeutic agent such as a COX-2 inhibitor or a GnRH agonist.

Heinrichs does not teach or suggest the use of etoricoxib or any other COX-2 selective inhibitor to treat endometriosis. In fact, Heinrichs does not teach or suggest the use of any compound to treat endometriosis. Instead, Heinrichs describes coadministration of an estrogen agent and a progestin agent to prevent endometriosis *signs and symptoms* (emphasis added). Applicants are claiming the treatment of endometriosis itself, not the signs and symptoms of endometriosis. These are different diseases/disorders. Therefore, Heinrichs' disclosure is not relevant to the field to which applicants' invention as set forth in claims 1, 22, 23, 25 and 26 is directed, and therefore, not prior art under 35 U.S.C. §103(a).

In addition, Heinrichs invention is directed to the coadministration of an estrogen agent and a progestin agent. Applicants' invention as set forth in claims 1, 22, 23, 25 and 26 do not recite coadministration of both an estrogen agent and a progestin agent. Instead, applicants' invention as set forth in claims 1, 22, 23, 25 and 26 recite the administration of either (i) a COX-2 inhibitor alone (claim 1); (ii) a COX-2 inhibitor with an oral contraceptive, such as a progestin agent (claims 22 & 23); or (iii) a COX-2 inhibitor and a GnRH-agonist (claims 25 and 26). Nowhere does Heinrichs teach or suggest the use of either a progestin agent alone or an estrogen agent alone, or either co-administered with a COX-2 selective inhibitor, to treat endometriosis.

As demonstrated above, there is simply no motivation or suggestion to combine the cited references to create applicants' claimed invention.

In view of the above remarks, applicants maintain that claims 1, 22, 23, 25 and 26 satisfy the requirements of 35 U.S.C. §103(a). Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection, and earnestly solicit allowance of the pending claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone her at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the large entity amount of such fee to Deposit Account No. 13-2755 referencing attorney docket number 21294P.

Respectfully submitted,

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